

## REMARKS

Claims 1-15 are pending, and claims 9-14 have been withdrawn from consideration. Claims 1-8 and 15 stand rejected on various grounds which are addressed below.

### Amendments

Claims 3 and 15 have been canceled without prejudice and disclaimer.

Claims 1, 2, and 5 have been amended to recite “isolated” in view of a requirement under 35 U.S.C. §101.

Claim 2 has been amended to:

(i) limit the protein of (a) to “an isolated protein comprising the amino acid sequence of SEQ ID NO: 2, wherein up to 10 amino acids are deleted, inserted and/or substituted with different amino acids, wherein said protein has protease activity”; and

(ii) cancel the protein of (b) without prejudice and disclaimer.

In addition, claim 2 has been amended to recite “wherein up to 10 amino acids are deleted, inserted and /or substituted with different amino acids”. Support for this amendment is found, for example, on page 8, lines 6-35 of the application. This claim has also been amended to include the limitation that “said protein has protease activity.” Support for this language appears, for example, on page 35, lines 21 to page 37, line 9 (Example 2).

Claim 4 has been amended to recite the preceding claims, and remove the terms of “first” and “a second,” and to recite “other” instead. Support is found, for example, on page 8, line 36 to page 9, line 21.

Claim 5 has been amended to independent form and to be drawn to DNAs encoding a protein of claim 1 or 2, or a DNA encoding a protein of claim 2(b) now canceled which has been defined by incorporating the limitations of claim 2(b) and also with a specific biological property. The limitation of “said protein has protease activity” finds support, for example, on page 35, line 21 through page 37, line 9 (Example 2).

Claim 6 has been amended to recite “comprising.”

Claim 7 has been amended to recite “transformed cell comprising”. Support for this amendment is found, for example, on page 12, line 17 through page 13, line 12.

Claim 8 has been amended to correct its dependency in view of the present claim amendments.

Withdrawn claims 9 and 11 have also been amended to correct dependency.

No new matter has been added by any of the aforementioned amendments.

#### Information Disclosure Statements

Applicants point out that Information Disclosure Statements were filed on September 4, 2001 and June 6, 2002. Copies of these Statements including return date-stamped postcards received from the PTO are also enclosed. Applicants note that the

Forms PTO 1449 which accompanied these Statements have not been initialed and returned, and hereby request that each be initialed and returned with the next Office action.

### Drawings and Specification

Applicants' drawings and specification have been objected to for disclosing sequences that were not identified by sequence identified numbers. Applicants note that the Reply to Notification to Comply with Sequence Requirements and Preliminary Amendments filed respectively August 3, 2001 and October 11, 2001 (copies enclosed) each addressed these issues. Applicants further point out that MPEP § 2429 states:

Figures can be used to convey information not readily conveyed by the Sequence Listing. The exclusive conformance requirement of 37 CFR 1.821(b) will be relaxed for drawing figures. However, the sequence information so conveyed must still be included in a "Sequence listing" and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the "Brief Description of Drawings."

Accordingly, with respect to the drawings, sequence identifiers may be used in either the drawings or in the "Brief Description of the Drawings". As Applicants' have complied with this standard, this objection should be withdrawn.

In addition, the Office has objected to Figure 12 because lanes 1-22 of this figure were not identified. Applicants respectfully point out that Example 8 (on page 44, line 31 through page 45, line 6) and the brief description of Figure 12 (on page 32, lines 30-31) clearly describe the lane numbers as corresponding to the number or kind of human

chromosomes , for example, chromosome 1, chromosome 2, chromosome 3 .... the X chromosome and Y chromosome. Applicants, in view of this clarification, accordingly believe no further action is required and respectfully request that this objection be withdrawn.

### Claims

Applicants' claim set was objected to for not beginning with a sentence of which the claims are an object. The present amendment to the specification corrects this issue. This objection should be withdrawn.

Claims 3 and 4 were objected to as including non-standard Markush language. The present amendment, canceling claim 3 and amending claim 4, addresses these issues, and this ground of rejection should be withdrawn.

### Rejection under 35 U.S.C. §101 and §112, first paragraph

Claims 1-8 and 15 stand rejected under 35 U.S.C. § 101 on the ground that “the claimed invention lacks patentable utility.” The Office alleges that

The specification fails to teach a specific and substantial function for the protein set forth by SEQ ID NO: 2, as encoded by SEQ ID NO: 1. Based on the specification, page 1, paragraph 1, the asserted utility for said protein is as a trypsin-family serine protease. Said assertion for the protein of SEQ ID NO: 2 is not supported by any experimental evidence; for example, analysis of the protein for protease activity. In addition, a utility for the protein of SEQ ID NO: 2 as a trypsin-like protease is not supported by homology to any protein with known function. Sequence searches by the Office failed to identify homology of SEQ ID NO: 2 with any protein having demonstrated trypsin-like activity.

The Utility Examination Guidelines (66 CFR 1092-1099) and Revised Interim Utility Guidelines Training Materials outline the criteria to determine the utility of an invention. The utility of an invention must be specific and substantial or well established. In defining the metes and bounds of a specific utility of a DNA molecule encoding a full Open Reading Frame, Example 10 of the Guidelines states:

**Example 10: DNA Fragment encoding a Full Open Reading Frame (ORF)**

**Specification:** The specification discloses that a cDNA library was prepared from human kidney epithelial cells and 5000 members of this library were sequenced and open reading frames were identified. The specification discloses a Table that indicates that one member of the library having SEQ ID NO: 2 has a high level of homology to a DNA ligase. The specification teaches that this complete ORF (SEQ ID NO: 2) encodes SEQ ID NO: 3. An alignment of SEQ ID NO: 3 with known amino acid sequences of DNA ligases indicates that there is a high level of sequence conservation between the various known ligases. The overall level of sequence similarity between SEQ ID NO: 3 and the consensus sequence of the known DNA ligases that are presented in the specification reveals a similarity score of 95%. A search of the prior art confirms that SEQ ID NO: 2 has high homology to DNA Ligase encoding nucleic acids and that the next highest level of homology is to alpha-actin. However, the latter homology is only 50%. Based on the sequence homologies, the specification asserts that SEQ ID NO: 2 encodes a DNA ligase.

**Claim 1:** An isolated and purified nucleic acid comprising SEQ ID NO: 2.

**Analysis:** The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? Based upon applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO: 2 encodes a DNA ligase. Further, DNA ligases have a well-established use in the molecular biology art based on this class of protein's ability to ligate

DNA. Consequently the answer to the question is yes.

Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed. In order to determine whether the claimed invention has a well-established utility the examiner must determine that the invention has a specific, substantial and credible utility that would have been readily apparent to one of skill in the art. In this case SEQ ID NO: 2 was shown to encode a DNA ligase that the artisan would have recognized as having a specific, substantial and credible utility based on its enzymatic activity. Thus, the conclusion reached from this analysis is that a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should not be made.

In the present case, Applicants' Example 3, found on page 37 of the application, describes the cloning of full-length cDNA of the "Tespec PRO-2" gene. Here Applicants point out that "Tespec PRO-2" polypeptide includes two signature protease motifs: the "Trypsin-His" motif and the "Trypsin-Ser" motif. Applicants further note that "the two motifs of "Tespec PRO-2" .... exhibit[] high homologies to known trypsin-family serine proteases." Figure 3 further shows the alignment of amino acid sequences of "Tespec PRO-2" and several known trypsin-family proteases such as acrosin, prostatic, and trypsin.

In sum, in view of Example 10 of the Utility Guidelines and Applicants' Example 3 in combination with Figure 3, the related rejections under 35 U.S.C. §101 and §112, first paragraph should be withdrawn.

#### Rejections under 35 U.S.C. §112, second paragraph

Claims 2-18 and 15 were rejected under 35 U.S.C. 112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Office asserts that the terms of “functionally equivalent” of claim 3, “the first protein” of claim 4, “transformant” of claims 7 and 8, and “hybridizing to” of claim 15 are indefinite. The Office further noted that claim 6 is indefinite because it is unclear whether the recited vector comprises the DNA according to claim 5 or is an empty vector into which the DNA will be inserted. Each of these issues is addressed by the present claim amendments, and the rejections should therefore be withdrawn.

#### Rejections under 35 U.S.C. § 112, first paragraph

##### Enablement

Claims 1-8 and 15 were rejected under 35 U.S.C. § 112, first paragraph on the ground that Applicants’ specification does not reasonably provide enablement for a protein that is functionally equivalent to a protein comprising SEQ IDNO:2, any fragment thereof, any encoding polynucleotide, or any polynucleotide of at least 15 bases that hybridizes to SEQ ID NO:1. As applied to the amended claims, this rejection should be withdrawn.

The standard for enablement is articulated in *In re Wands* 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). In defining the boundaries of undue experimentation, the *Wands* court stated that “the key word is ‘undue’ not ‘experimentation’” and that “the

test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine.” *Id.* at 737. Applicants’ specification meets this standard.

Like the practitioners of the monoclonal antibody art described in *Wands*, who screened many hybridomas to isolate the one having the desired characteristics, practitioners in the art of molecular biology are prepared to screen many molecules to find one that contains a desired property. Such screening of molecules falling within Applicants’ claims is considered to be a routine step in the process of isolating molecules having the desired characteristics; it cannot constitute undue experimentation.

As the case of *In re Wands* (858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988)) makes clear, enablement is not negated by the necessity for some experimentation such as routine screening. The present invention, like *In re Wands*, may involve screening. As stated *In re Wands*, “a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” In light of the teaching of the specification, screening nucleic acids for protease activity or having the required hybridization characteristics might be laborious, but would not require undue experimentation.

This basis for the rejection under § 112, first paragraph should therefore be withdrawn.



### Written Description

The Office asserts that Applicants' specification does not contain any disclosure of the function of all the claimed polypeptides and fragments thereof or of the polynucleotides encoding such polypeptides. This rejection should be withdrawn.

Claim 1, as amended, reads:

An isolated protein comprising the amino acid sequence of SEQ ID NO: 2.

Claim 2, as amended, recites:

An isolated protein comprising the amino acid sequence of SEQ ID NO: 2, wherein up to 10 amino acids are deleted, added, inserted and/or substituted with different amino acids, wherein said protein has protease activity.

Claim 5, as amended, reads:

An isolated DNA selected from the group consisting of:

- (a) a DNA comprising the nucleotide sequence of SEQ ID NO: 1;
- (b) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2;
- (c) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, wherein up to 10 amino acids are deleted, added, inserted and/or substituted with different amino acids, and wherein said protein has protease activity; and
- (d) a DNA which hybridizes under the stringent conditions of 42°C, 2xSSC, 0.1% SDS to the complement of a DNA comprising the nucleotide sequence of SEQ ID NO: 1, wherein said protein has protease activity.

The specification as filed meets the written description requirement for the language recited in the amended claims. See, for example, page 8, lines 6-36 of the specification, as well as page 35, line 21 through page 37, line 9 (Example 2). In view of this description, Applicants' specification clearly satisfies the written description

requirement, and Applicants request reconsideration and withdrawal of this basis for the § 112 rejection.

Applicants further point out that the Guidelines for Examination of Patent Applications Under 35 U.S.C. 112 ¶1, “Written Description” Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) state:

[f]actors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.

As noted above, the claimed proteins are distinguished from other proteins by both the structural characteristic of including amino acids of SEQ ID NO:2 and by the specific functional characteristic of having protease activity (Claim 1). Similarly, the claimed proteins including the amino acid sequence of SEQ ID NO: 2, wherein up to 10 amino acids are deleted, added, inserted and/or substituted with different amino acids, wherein said protein has protease activity proteins are also distinguished from other proteins.

Based on Applicants’ disclosure of these properties and routine assays for determining whether a particular protein has these properties, one skilled in the art would appreciate that Applicants were in possession of the claimed invention. Furthermore, there is no

question that the claimed DNAs (claim 5) encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, wherein up to 10 amino acids are deleted, added, inserted and/or substituted with different amino acids, and wherein said protein has protease activity are distinguished from other proteins by both the structural characteristic and by the specific functional characteristic of having protease activity.

Finally, Applicants note that the present claims are also in compliance with the Written Description Guidelines as exemplified by Examples 9 and 14.

For all of the aforementioned reasons, Applicants respectfully request that the section 112, written description rejection be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claim 3 was rejected under 35 U.S.C. § 102(b) as anticipated by Sigma, Inc. (1997). As claim 3 has been canceled, this rejection is now moot.

## CONCLUSION

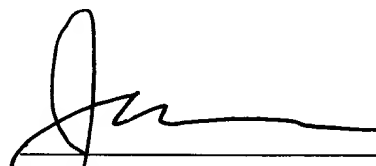
Applicants submit that the claims are in condition for allowance, and such action is respectfully requested.

Enclosed is a Petition to extend the period for replying to the Office action for three (3) months, to and including November 24, 2006 as November 23<sup>rd</sup> was a Federal Holiday.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 24 November 2006

  
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